UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/358,103	07/21/99	ROCA A	ROCA-01

HM12/0510

R PERRY MCCONNELL
10655 SIX PINES
SUITE 130
THE WOODLANDS TX 77380

EXAMINER	
FRONDA, C	
ART UNIT	**PAPER NUMBER**
1652	10

DATE MAILED: 05/10/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/358,103	Applicant(s) Roca
	Examiner Christian L. Fronda	Group Art Unit 1652

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-27 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-27 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The meaning of the phrase "In an *E. coli* RecA protein or a protein having a MAW motif homologous to the *E. coli* MAW motif, a RecA homolog protein mutant" is uncertain because it is not known what protein the claim is directed to.

Claims 1-27 are under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The amino acid residue positions recited in these claims do not correspond to SEQ ID NO:1. The claims recite positions such as residue 43, 52, and 53. However, SEQ ID NO:1 is a sequence consisting of only 26 amino acid residues. Appropriate correction is required which specifically refers to the position of the amino acid residues of SEQ ID NO:1.

Claim Rejections - 35 U.S.C. § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-27 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The specification asserts that mutant RecA proteins containing mutations in the MAW motif have different properties from the wild type RecA protein. The specification asserts that such mutants do not require the cofactor ATP γ S to function and that such property is economically beneficial in applications requiring RecA. In addition the specification asserts that such mutants have tighter binding to DNA than wild type RecA. The specification teaches how to construct RecA mutants having mutations in the MAW motif. However, working examples

are not present in the specification which compare the functions of wild type RecA and mutant RecA protein in the presence or absence of ATP γ S or other nucleoside triphosphate cofactors or working examples which compare the DNA binding activity of mutant RecA protein to wild type RecA protein. Furthermore, no working examples are present which support the assertion that mutant RecA proteins require no nucleoside triphosphate cofactors in order to function or have tighter binding activity toward DNA. Hence, the invention is not supported by a credible asserted utility.

Claims 1-27 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Zarling *et al.* Claims 1, 2, 8, and 9 are anticipated by Zarling *et al.* because Zarling *et al.* teach a RecA protein that has an arginine residue, which is volumetrically larger than glycine, at the position corresponding to post 43 of the *E. coli* MAW motif (see **Alignment 1**).

Claims 4, 15, and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Garcia. Claims 4, 15, and 21 are anticipated Garcia since Garcia teach a RecA protein that has an isoleucine residue at the position corresponding to position 53 of the *E. coli* MAW motif and a phenylalanine residue at position 60 of the *E. coli* MAW motif (see **Alignment 2**).

Claims 7 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by McKean *et al.* Claims 7 and 14 are anticipated by McKean *et al.* since McKean *et al.* teach a Dmc1 protein which is homologous to bacterial RecA protein and has an arginine residue at the post

corresponding to position 59 of the *E. coli* MAW motif (see **Alignment 3**).

Claims 16 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ramesar *et al.* Claims 16 and 22 are anticipated by Ramesar *et al.* since Ramesar *et al.* teach a RecA protein that has a tryptophan residue at the post corresponding to position 40 of the *E. coli* MAW motif (see **Alignment 4**).

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konola *et al.* in view of Story *et al.* (1993), Story *et al.* (1992), and Menetski *et al.*

Konola *et al.* teach a *recA* gene inserted into a plasmid and a method to assay for RecA activity in vitro (see entire publication). Konola *et al.* do not teach RecA proteins or homologs containing mutations at the MAW motif. Story *et al.* (1992) teach the crystal structure of the RecA protein-ADP complex, and that binding of nucleoside triphosphate to the *E. coli* RecA causes a conformational change in the RecA protein which activates it and stimulates binding to DNA (see entire publication). Story *et al.* (1993) teach class IV residues which are part of the MAW motif. Menetski *et al.* teach an assay for measuring the binding activity of RecA protein (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a RecA protein or homolog of a RecA protein according to claims 1-27 because the crystal structure of RecA is known, a conformational change in RecA which activates RecA is known, class IV residues are known, and assays for measuring RecA activity are known. Producing mutants having the enhanced property of tighter DNA binding or no requirement for nucleoside triphosphate cofactors is expected to be accomplished by modifying the teachings of Konola *et al.* in the following manner:

A. Because Story *et al.* (1992) teach the crystal structure of the RecA protein-ADP complex

and that ATP binding induces a conformational change which stimulates binding to DNA; and Story *et al.* (1993) teach class IV residues which are part of the MAW motif, modify amino acid residues in the MAW motif of the RecA protein taught by Konola *et al.* or homolog so that this modification changes the conformation of the RecA protein or homolog in the same manner ATP induces a conformational change. Modification of amino acid residues include substitution with amino acid residues that are volumetrically larger than the wild type amino acid residues or substitution with aromatic amino acid residues or conservative substitutions.

B. Mutate the DNA encoding the RecA protein as taught by Konola *et al.* or homolog by site-directed mutagenesis which is a well known method in the art.

C. Express and purify mutants according to the teachings of Guan *et al.*

D. Screen for mutants having activity in the absence of nucleoside triphosphate cofactors by using the assy method taught by Konola *et al.*

E. Screen for mutants having tighter binding to DNA by using the assay method taught by Menetski *et al.*

Because RecA and proteins homologous to RecA are involved in repairing damaged DNA, one of ordinary skill in the art would be motivated to make RecA mutants or homologs of RecA mutants with enhanced properties for use in homologous recombination based gene therapies.

Conclusion

4. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF
May 1, 2000

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600